



Infectious Disease Epidemiology Section
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ENCEPHALITIS

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The term encephalitis refers to inflammation of the brain. Because meningeal inflammation often accompanies these inflammatory processes, compounded terms such as meningoencephalitis and meningoencephalomyelitis are sometimes used.

Etiology

Arboviruses include three families of viruses:

1- Alphaviruses: Eastern equine, Western equine and Venezuelan equine encephalitis. Eastern Equine Encephalitis (EEE) is the most common alphaviral encephalitis in Louisiana with a few sporadic cases every few years.

2- Flavivirus: West Nile (WN) and St. Louis Encephalitis are the most common causes of flavivirus encephalitis in Louisiana. Dengue encephalitis is a rare complication.

3- Bunyavirus: Few cases of La Crosse virus are observed every year in Louisiana. Rift Valley Fever is not observed in the USA but is a major concern because of the possibility of importation.

Enteroviruses are a common cause of viral or aseptic meningitis but occasionally may cause encephalitis. They include coxsackievirus and echovirus.

Adenovirus, viruses of mumps, measles, lymphocytic choriomeningitis are also more common causes of meningitis than of encephalitis.

Rabies virus is typically causing an encephalitis.

Herpesvirus causing encephalitis include herpes simplex virus types 1 and 2, varicella-zoster virus, Epstein-Barr virus, Cytomegalovirus and human herpesvirus 6.

Epidemiology

Passive reporting systems underestimate the incidence of viral encephalitis. Reported incidence is around 0.3 to 0.6/100,000. However special surveys show that the true incidence is about twice that rate. Herpes simplex virus CNS infections occur without seasonal variation, affect all ages and constitute the majority of fatal cases of endemic encephalitis in the USA.

Clinical Description

An encephalitis is often preceded by a prodrome that includes a non specific febrile illness with headache, low grade fever, chills, malaise, anorexia, vomiting and abdominal pain. None of these signs or symptoms are specific. They could be observed in a number of infectious diseases.

Rashes that precede the encephalitis may give some important clues for the etiologic diagnosis. Lyme disease, Rocky Mountain spotted fever (palms and soles), typhus, varicella, herpes B virus, and herpes

zoster encephalitis are preceded by a rash. An exanthem is also occasionally seen with *Mycoplasma*, coxsackievirus, and echovirus infections. A history of tick bite is often obtained in Rocky Mountain spotted fever, Lyme disease, ehrlichiosis, and Colorado tick fever. A history of animal or bat bite may be obtained in rabies.

Infections limited to the leptomeninges manifest with signs and symptoms of meningeal irritation: headache, stiff neck, and pleocytosis.

Patients with viral encephalitis usually have signs and symptoms of meningeal inflammation, but, in addition to headache, fever, and nuchal rigidity, their encephalitis is characterized by alterations of consciousness: mild lethargy may progress to confusion, stupor, and coma. These may be accompanied by:

- Focal neurologic signs
- Seizures
- Motor weakness, accentuated deep tendon reflexes, and extensor plantar responses
- Abnormal movements, or a tremor characteristic of Parkinson's disease may develop.
- Hypothalamic pituitary axis involvement causes severe hyperthermia or poikilothermia, diabetes insipidus, and inappropriate antidiuretic hormone secretion.
- Spinal cord involvement leads to flaccid paralysis, depression of tendon reflexes, and paralysis of bowel and bladder
- Increased intracranial pressure can cause papilledema and third and sixth cranial nerve palsies

Altered mental status is classified according to the following steps.

	Response to			
	Noxious stimuli	Voice commands	Awake Eyes open	Alert
Coma	No	No	No	No
Stupor	Yes	No	No	No
Drowsiness	Yes	Yes	No	No
Confusion	Yes	Yes	Yes	No

Signs of herpes simplex encephalitis include personality change, hallucinations, and aphasia, due to the temporal lobe localization typical of that infection.

With Lyme neuroborreliosis, both peripheral nervous system and CNS complications occur, ranging from severe meningoencephalitis to isolated cranial nerve palsies.

The differential diagnosis includes

- Seizures;
- Brain abscess, subdural empyema: Focal lesions, high cell count (>50,000)
- Bacteremia and sepsis, endocarditis with embolic infarction in brain
- ADEM (acute disseminated encephalomyelitis) or Post infectious encephalomyelopathy: measles, mumps, varicella;
- Viral syndrome (influenza)
- Post vaccinal reactions: rabies (Semple type vaccine), smallpox
- Cerebral malaria; trichinosis; cysticercosis; toxocariasis; trypanosomiasis
- Carcinomyes openatous meningitis, meningeal leukemia

Laboratory Tests

CSF examination is essential. The pleocytosis of viral encephalomyelitis is variable (10 to 2000 cells/mm³), and mononuclear cells usually predominate; however, early in any of these diseases there may be no cells, or polymorphonuclear cells may be present in considerable numbers.

The main characteristics of the CSF are:

- Increased pressure: Abnormal > 150 mmH₂O; >450mm = acute brain swelling
- Cell count: Few (10) or at most 1,000; rarely up to 8,000; mostly mononuclear; neutrophils may predominate in early stages. Repeat examination of the CSF in 24 hours is often useful.
- Glucose: Normal (compare with blood level in diabetics) or mildly depressed (80% of blood);
- Protein: < 100-150mg /dL, up to 500; >1,000 in subarachnoid blockage
- Bacteriology: Gram stain negative; Culture negative; No bacterial antigens
- Virology: CSF viral cultures
- Blood cultures negative
- EEG: Slowing of background rhythms; focal or diffuse epileptiform discharges; some focal abnormalities (40% CE children; 50% EEE); Deep depression of background activity in severe cases
- MRI allows better visualization of the spinal cord, is a sensitive indicator of demyelination, and can detect the edematous changes that are often an early feature of encephalitis.

Serology

Single sample of serum or CSF for IgM: CE, EEE, WEE, SLE, JE

Rise in IgG antibody over paired sera collected at 6 weeks interval:

Most patients with rabies have detectable serum antibodies by day 15 of their illness.

Virology:

CSF, throat washings, or stool for enteroviruses;

Urine and saliva for CMV;

CSF, blood, throat washings, rectal swab, urine, fluid from skin lesions,

CNS tissues obtained by biopsy or autopsy for unknown

PCR PCR used to detect in CSF: DNA from HSV, CMV, VZV, EBV, JE virus,
RNA from rabies virus, HIV, enteroviruses